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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/875,440	06/05/2001	Christoph Reinhard	PP-01701.002	5034

7590 01/13/2003

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EXAMINER	
MCGARRY, SEAN	
ART UNIT	PAPER NUMBER
1635	9

DATE MAILED: 01/13/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

FILE COPY

Office Action Summary	Application No.	Applicant(s)	
	09/875,440	REINHARD ET AL.	
	Examiner	Art Unit	
	Sean R McGarry	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 October 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) *2-5,11,13-16,18 and 21-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 6-10, 12, 17, 19, 20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 4,5 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicant's election with traverse of Group IV in Paper No. 8, filed 10/28/02 is acknowledged. The traversal is on the ground(s) that claim 20 has not been attributed to a group and that claims 12, 17, 19, and 20 should be examined with Group IV since these claims are generic to the elected claims. This specific argument is agreed with and claims 1, 6, 7, 8, 9, 10, 12, 17, 19 and 20 are under examination. Claims 1, 9, 10, 12, and 19 are generic to the invention and will be examined as far as they read on the elected invention. Applicant has not offered any other arguments other than those addressed above. The restriction requirement is otherwise still deemed proper and is therefore made FINAL for those reasons set forth in the Restriction mailed 9/27/02.

Claims 2-5, 11, 13-16, 18, 21-23 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 8. In view of the above, applicant should amend the claims such that they read only on that subject matter elected.

Claims 1, 6-10, 12, 17, 19, and 20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making antibodies to NET-4, does not reasonably provide enablement for making or using therapeutically effective amounts of Net-4 antibody modulators. The specification does not enable any

person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The instant invention is drawn to therapeutically effective NET-4 modulators which are antibodies to NET-4 and methods of treating disease with such modulators.

The instant specification discloses that the prior art indicates that the function of NET-4 is not known. The instant specification does not provide an indication of the function of NET-4 but shows that NET-4 mRNA is over expressed in 83% of colon cancer cells tested. The specification shows that inhibition of NET-4 mRNA with various antisense causes an inhibition of cell proliferation in colon cancer cell, for example.

It is clear that one in the art could easily make an antibody to NET-4, which protein has been disclosed in the prior art (Serru et al. Biochimica Acta Vol. 1478:159-163, 2000), by known and routine methods known in the art and reviewed in the instant specification, however, the instant claims require that the instantly claimed antibodies be modulators of NET-4 function. That is, they must be able to increase as well as inhibit NET-4 activity, and in some embodiments function as therapeutic compounds, for example.

The instant specification discloses inhibition of NET-4 mRNA via antisense oligonucleotides. The instant specification does not show increased function of NET-4 via antisense oligonucleotides, for example.

The specification provides ample guidance for one to make antibodies at pages 13-17, for example, but nowhere is it shown or taught how to make and use antibodies that increase NET-4 activity.

One in the art is left to perform undue trial and error experimentation to make and determine how to use antibodies that function as agonists of NET-4 function, for example, and even further, an antibody that functions as both an antagonist and an agonist (i.e. a modulator). The instant specification provide no more than art known methods for making antibodies, but no specific guidance such that one in the art could make an antibody modulator, for example. The specification does not point to the prior art to show one how to make antibodies that are modulators.

It is noted that the instant specification discloses no antibodies of NET-4 in the instant specification. There is no disclosure of an antibody that inhibits function of NET-4, no antibody that increases NET-4 function and no antibody that possesses both agonistic and antagonistic properties, for example.

The specification appears to base the enablement of antibody modulators on the antisense examples in the specification. Antisense oligonucleotides function to inhibit NET-4 mRNA expression and antibodies typically function by binding to a protein which potentially creates an antibody that inhibits function of a protein. It is unclear how these would correlate. First it is not clear that such a correlation can be drawn since, for example, antisense target nucleic acids and antibodies target proteins. The instant specification teaches that NET-4 is over expressed in colon cancer cells. It has not been demonstrated by the instant specification that the increase in NET-4 mRNA levels is a cause of the colon cancer phenotype or a consequence thereof, for example. The instant specification does not show that there is a correlation of increased NET-4 protein in the cells. It is known in the art that there is no simple correlation between mRNA

levels and protein levels (see Anderson et al Electrophoresis Vol. 18:533-537, 1997, for example). Furthermore even the antisense examples provided do not show that inhibition of NET-4 selectively inhibits the growth of cancer cell since there has been no data provided that shows that normal or different cell types (other than colon cancer cell , or cells that do not over express NET-4 mRNA) are not also inhibited in the growth more less or equal to those colon cancer cells. One in the art is clearly left to perform large quantities of undue experimentation to address those concerns indicated above in order to make and use the instant invention as claimed.

The instant specification simply does not teach how to make antibody modulators, does not provide a disclosure of specific embodiments that demostrat antibodies with such properties, or disclose any example that would show by correlation, antibodies that function as modulators or how to use such modulators in a method of treating disease.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sean R McGarry whose telephone number is (703)305-7028. The examiner can normally be reached on M-Th (6:00-4:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader can be reached on (703) 308-0447. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

SRM
January 9, 2003